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# Enteral Nutrition as a Life-Saving Treatment in Patients with Severe Anorexia Nervosa

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## 1. Introduction

Anorexia Nervosa is a serious, potentially life-threatening illness characterized by severe malnutrition, with abnormally low body weight (BMI  $<17.5$  kg/m<sup>2</sup> or body weight at least 15% below the expected value), an intense fear of weight gain, and an undue emphasis on weight and shape in self-evaluation. Amenorrhea (i.e. loss of three consecutive menstrual cycles) is currently required for the diagnosis, but often is hidden by contraceptive drugs. Anorexia nervosa can cause significant clinical complications in every organ system, particularly relevant in adolescents in the growing and developing body with slowing in linear growth, impaired bone mineral accretion, structural and functional damage of the brain. Most of these complications are reversible if there is a timely restoration of body weight, since weight restoration is associated with concomitant decrease in anorectic symptoms and an improvement in physical and cognitive function (American Academy of Pediatrics. Committee on Adolescence. Identifying and treating eating disorders. Pediatrics, 2003; American Dietetic Association, Nutrition intervention in the treatment of eating disorders, 2011; American Psychiatric Association. Work Group on Eating Disorders. Practice Guideline for the treatment of Patients with Eating Disorders. 2006; Beumont, 2004; Eating Disorders. Core Interventions in the treatment and management of anorexia nervosa, bulimia nervosa and related eating disorders. National Institute for Clinical Excellence, 2004).

Weight restoration is also a prerequisite for psychotropic interventions and effective use of psychotherapeutic therapy (Eating Disorders. Core Interventions in the treatment and management of anorexia nervosa, bulimia nervosa and related eating disorders. National Institute for Clinical Excellence, 2004; Stanga et al., 2007).

Moreover, we also must consider that anorexia nervosa patients display the highest death rate of all mental illnesses and a relevant part of mortality has to be attributed to undernutrition.

If undernutrition is severe, patients are at high risk, and medical complications affect virtually every organ system. Severely undernourished patients, if not appropriately treated with a specialized in-patient care program, may present cardiovascular, metabolic complications, and abnormalities in brain functions, and it is not infrequent for these complications to require treatment in intensive care units, thus extending hospitalisation time and consequently increasing costs (Golden & Meyer, 2004; Gentile et al., 2008).

Severe and protracted undernutrition nearly always leads to marked changes in body spaces (e.g. intra-extracellular water), in body masses (e.g. potassium, phosphate, magnesium overall and compartmental stores), in equilibrium relationships between bodily spaces, concentrations and in feedback mechanisms which are set at new-pathological levels of functioning. These changes set the body at risk of refeeding syndrome, i.e. the disturbances caused by a too rapid / or unbalanced refeeding which the deranged bodily system just referred to be unable to support (Mehanna et al., 2008).

Several guidelines, papers and reviews provide guidance for medical and nursing staff managing patients with severe undernutrition and/or at risk of refeeding syndrome. There are also many reports of medical complications in refeeding anorexia nervosa patients (Stanga et al., 2008; Marinella et al., 2005; Hearing, 2004; Birmingham, 2008).

So, caring for severely starved patients with anorexia nervosa and re-starting nutrition commands close monitoring seeking for early signs or symptoms of refeeding and specialized care operating, within a timely plan, both at a physical (first) and emotional level (successively), the final goal being to restore a healthy, self managing person to her/his family and social environment (Gentile et al., 2010).

Until now there has been no category A evidence for treatment of anorexia nervosa, but international guidelines and society position papers agree in defining the best treatment as a multidisciplinary, comprehensive and rigorous process conducted by a team of medical, nutritional, mental health and nursing professionals, experienced in the evolution and treatment of eating disorders (American Academy of Pediatrics. Committee on Adolescence. Identifying and treating eating disorders. Pediatrics, 2003; Eating Disorders. Core Interventions in the treatment and management of anorexia nervosa, bulimia nervosa and related eating disorders. National Institute for Clinical Excellence, 2004).

Usually Centres that treat inpatient anorexia nervosa who have moderate or severe degrees of undernutrition use a combination of behavioural techniques, cognitive restructuring and a progressive structured program of oral caloric intake to achieve the goal of weight restoration. In the more complicated cases i.e. patients with extreme undernutrition and life threatening weight loss or patients unwilling to take dietary treatment or refusing oral intake, artificial nutrition has been utilized (Table 1).

Patient with severe malnutrition (BMI $\leq$ 13 Kg/m <sup>2</sup> ) disposed to intake less than 100% of the caloric needs or patients with body weight not increasing
Patient with BMI between 13 -15 Kg/m <sup>2</sup> showing a reduction of measured resting metabolic rate more than 30% of exstimated basal metabolic rate according to Harris Benedict formula.
Patient unwilling to take dietary treatment or refusing any oral intake but accepting only Artificial Nutrition.

Table 1. Criteria for life-saving intervention with artificial nutrition in anorexia nervosa patients

Although it has always been stressed how crucial nutritional rehabilitation is in these patients, where only few studies are reporting the use of artificial nutrition in anorexia nervosa patients. Enteral nutrition and parenteral nutrition are both used in nutritional

rehabilitation of severe anorexia nervosa patients (Paccagnella et al., 2006; Robb et al., 2002; Tonoike et al., 2004; Zuercher et al., 2003; Gentile et al., 2008; Gentile et al., 2010).

Given the recognised difficulties in conducting randomized clinical trials in patients with anorexia nervosa, evidence-based guidelines for enteral and parenteral nutrition are lacking. If we apply the international guidelines for the use of artificial nutrition (“if guts work you must use it”) also in those anorexia nervosa patients who require life-saving intervention with artificial nutrition, we must choose enteral nutrition while parenteral nutrition should be considered only for very rare patients with impaired intestinal function (Lochsa et al., 2006; Bankhead et al., 2009) (Table 2).

<p>Enteral tube feeding should be considered in people who are malnourished and have inadequate or unsafe oral intake and a functional accessible gastrointestinal tract.</p> <p><b>Reducing contamination</b></p> <p>Use of sterile, non-manipulated closed systems for enteral tube feeding administration and good hygiene, along with routine microbial surveillance reduce contamination associated with preparation. The use of closed system enteral administration set has been demonstrated to be safe for 24 hours.</p> <p><b>Enteral formula stability</b></p> <p>The stability of each component of an enteral tube feeding formula is important to maintaining the product’s integrity and the patient’s nutrition status.</p> <p><b>Selection of Enteral Access Devices</b></p> <p>In general gastric access relies on a functional stomach free of delayed gastric emptying obstruction or fistula. Small bowel feedings are most appropriate for patients with gastric outlet obstruction gastroparesis, pancreatitis and in those with known reflux and aspiration of gastric contents. Enteral access devices inserted via the nasal routes are usually placed for short-term use in the hospitalized patient.</p>
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Table 2. Indication for enteral tube feeding and practice recommendation

Enteral feeding must be closely monitored and regulated via a electronically operated pump. Nasogastric feeding is the preferred procedure in many eating disorders units, because it is a safe and simple non surgical procedure that can be performed also by nursing staff. Compared with other methods of refeeding nasogastric feeding has a lower risk of complications and is cost-efficient.

The aim of this retrospective cohort study is to describe our experience with the use of enteral tube feeding for gradual correction of severe undernutrition in anorexia nervosa patients according to main international guidelines for the use of artificial nutrition and to available studies and clinical experience that support the effectiveness of enteral nutrition in weight restoration.

2. Patients and methods

2.1 Patients

We treated 122 (118 females, 4 males) inpatients, referred to the Eating Disorders Unit of Niguarda Hospital and affected by severe undernutrition due to anorexia nervosa (according to the Diagnostic and Statistical Manual of Mental Disorders, 2000), treated with nasogastric enteral nutrition. The observation period was from May 1999 to January 2011.

## 2.2 Measurements

### 2.2.1 Anthropometry and resting metabolic rate

Body weight was recorded to the nearest 100 g, using a standard physician's weight scale with patient wearing only underwear (without shoes). Height was determined to the nearest 0.5 cm on a standard stadiometer.

Resting gas exchange was measured by open circuit, indirect calorimetry (Sensor Medics) for 30 minutes. Before each measurement, the system was re-calibrated using a reference gas mixture of 95% O<sub>2</sub> and 5% CO<sub>2</sub>.

## 3. Treatment

Our multidisciplinary treatment consist in:

- a. Behavioural and psychological therapy for patient and their parents.
- b. Nutritional rehabilitation to restore weight correcting biological and psychological consequences of undernutrition.

Usually caloric intake levels were established beginning with indirect calorimetric measurements because resting energy expenditure is the main component of daily expenditure particularly in severely malnourished patients.

For severely malnourished patients, our nutritional rehabilitation program includes temporary supplementation with liquid food supplements, or - in life-threatening situations - temporary nasogastric feeding.

In our experience, enteral nutrition is necessary only in a minority of inpatients with a relevant degree of malnutrition and for a limited period of time. Enteral nutrition must always be integrated in a multidisciplinary approach, and managed by an expert team. In order to reduce gastric discomfort, it is usually administered via a nasogastric feeding tube and consists of a polymeric diet free of lactose and gluten, with a high degree of calories, a high nitrogen, complete fluid formula. The flow rate is maintained constant with a pump, during all infusion time (Table 3).

Enteral nutrition was used until the patients were no longer at life-risk and they started to collaborate with the treatment, increasing oral food amounts to a significant amount.

Dietary management was devised to achieve also behavioural modifications, patients were encouraged – not forced to eat enough to restore their weight.

Vitamin supplementation started just before feeding and continued during refeeding days.

Electrolyte levels were measured and if necessary supplemented. Phosphate supplements were administered unless blood levels were above normal values.

### 3.1 Data analysis

Data were analyzed with the SAS PACKAGE (Release 8.2 by SAS Institute Inc. Cary NC USA, 2002). The results are reported as means  $\pm$  Standard Deviations or frequencies and percentages. Changes in body weight and body mass indexes at admission and those after enteral nutrition treatment were tested with the sign test for paired data. The hypothesis of

<b>Formula</b>		
Calorie dense	1,7 - 2 Kcal/ml	
<b>Delivery site</b>		
Route	Access	
Gastric	Nasogastric	
<b>Method of Administration</b>		
Method		
Pump - assisted	Rate	20 - 30 ml/h 40 - 50 ml/h or more if tolerated, start with a 24-hour per day and proceed with a drop infusion for 18-12-8 hours per day if tolerated.
	Initial	
	Advance to goal of	
<b>Other indications</b>		
Flush the feeding tube with indicated amount of water every 6 - 8 hours		
No interruption of oral feeding if it is accepted		
<b>Monitoring</b>		
Check gastric residual volume according individual necessity		
Observe for abdominal distension, nasogastric tube site and assessment at least twice a day		
<b>Weight daily</b>		

Table 3. Specific enteral nutrition protocol for Anorexia Nervosa patient

no difference between the body weight and the body mass index at admission and after enteral nutrition treatment was rejected by a  $p < 0.0001$  for both variables.

4. Results

One hundred twenty-two patients were eligible for the study. Mean BMI was  $13.1 \pm 1.6$  kg/m<sup>2</sup> and the mean age was  $23.7 \pm 9.7$  years. A summary of patients’ anamnestic, demographic and clinical characteristics are reported in Table 4.

	Mean	S.D.	Range
Number of patients	122		
Age at reported onset/ diagnosis of Anorexia Nervosa	18.8	6.7	( 10.0 - 42.0)
Duration of disease (months)	54.4	64.1	( 2 - 356)
Age at beginning of enteral nutrition treatment (years)	23.7	9.7	(10 - 64)
Body Mass index (kg/ m <sup>2</sup> ) at beginning of enteral nutrition	13.1	1.6	(9.7 - 18.6)
Body weight (kg) at beginning of enteral nutrition	34.4	6.2	(19.5 - 63.8)
Height (cm)	162	0.1	(137 - 185)
Estimated resting metabolic rate (Kcal/ 24 h)	1166	120.5	(826 - 1724)
Measured resting metabolic rate (Kcal/ 24h)	860	160.5	(580 - 1356)
% difference versus estimated basal metabolic rate according to HB formula	-25.7	12.3	(-47 - 9)

<sup>a</sup> Values are means ± SDs, range in parenthesis

Table 4. Anamnestic, demographic and clinical data of Anorexia Nervosa patients treated by Enteral Nutrition <sup>a</sup>



We observed a clinically significant reduction in measurement resting metabolic rate ( $- 25.7 \pm 12.3\%$ ) respect to estimated basal metabolic rate according to Harris Benedict formula.

Table 5 presents the results of 122 anorexia nervosa patients treated with enteral nutrition. These patients continued to be treated by enteral nutrition till the achievement of BMI  $16.4 \pm 1.35 \text{ kg/m}^2$  ( $t=1$ ). Mean body weight increased from  $34.4 \pm 6.2 \text{ kg}$  to  $43 \pm 0.5 \text{ kg}$  after  $96 \pm 91$  days of enteral nutrition treatment with a mean enteral caloric supply of  $1378 \pm 261 \text{ Kcal}$ ; oral diet was never stopped. Patients and dieticians, together, selected a menu each day. Dieticians helped patients choose their own meals and provided a personalized, structured meal plan, which ensured nutritional adequacy and the inclusion of all major food groups.

Nasogastric tube feeding was continuously delivered over 24 h daily for the first 20-30 days, using feed pumps also to reduce gastric discomfort; as clinical conditions improved we proceeded with a drop infusion of 18-12-8 hours per day. We used a caloric dense completely fluid-formula diet, high nitrogen with protein intake of  $1.63 \pm 0.3 \text{ g/kg/body weight}$ .

	T = 0	T =1	T =2
N	122		
Body weight (kg)	$34.4 \pm 6.2$	$43.0 \pm 5.5^a$	$47.4 \pm 7.4$
Body mass index (kg/m <sup>2</sup> )	$13.1 \pm 1.6$	$16.4 \pm 1.35^a$	$18.0 \pm 2.5$
Duration Enteral Therapy (days)		$96 \pm 91$	
Enteral feeding regimen Kcal/day		$1378 \pm 261$	
Amount of fluid enteral diet ml/day		$707 \pm 181$	
Amount of fluid enteral diet ml/hour		$29 \pm 8$	
Caloric dense amount Kcal/ml		$1.9 \pm 0.2$	
Protein g/day		$56.1 \pm 13.9$	
Protein g/kg Body weight		$1.63 \pm 0.3$	
$\Delta$ weight (kg)		$8.7 \pm 4.4$	$12.8 \pm 7$
$\Delta$ weight /month (Kg)		$3.6 \pm 2.0$	$0.7 \pm 1.0$

T=0 onset of Enteral Nutrition Treatment, T=1 at end Enteral Nutrition Treatment, T=2 at the last out patient check after  $599 \pm 670$  days  
<sup>a</sup> significantly different from  $t=0$

Table 5. Clinical variables of 122 anorexia nervosa inpatient treated by enteral nutrition

We started slowly and we gradually increased the caloric intake during the first week to avoid refeeding syndrome.

5. Conclusion

Enteral nutrition was well tolerated and in those inpatients with severe, life-threatening undernutrition did not present any major complications, neither gastrointestinal complications such as diarrhea, vomiting, nor metabolic alterations such as hypoglycemia or hypophosphoremia nor hepatic malfunction.

If enteral feeding is integrated in a psychotherapeutic, empathic medical, nursing and dietitian approach the patients initially oppose it, but then, their compliance and co-operation is generally reasonable.

We choose to use enteral nutrition because we considered parenteral nutrition is more dangerous for developing a refeeding syndrome, and we agreed that parenteral nutrition should not be necessary for nutritional rehabilitation in Anorexia nervosa patients unless there is significant gastrointestinal dysfunction. In the group of 122 patients we never used it. In more severe patients we used infusion of 5-10% glucose fluid delivered during 24 hours a day until the metabolic alterations improved. The caloric intake was very gradually advanced in the first weeks to prevent the refeeding syndrome in those patients who are considered to be in high risk of refeeding syndrome. Prevention of refeeding syndrome is of crucial importance. The refeeding syndrome, a potentially lethal complication of refeeding the malnourished patient, can result in potential metabolic and pathophysiological complications, which can affect the cardiac, respiratory hematological, hepatic and neuromuscular systems leading to clinical complications and even death.

We choose to start with a 24 hour continuous flow supplement to reduce gastric discomfort, diarrhea and metabolic alterations, and only when the undernutrition was partially corrected, we gradually reduced the infusion time.

Our results seem to provide strong support for using a highly structured program for treating patients with severe anorexia nervosa; highly specialized eating disorder inpatient treatment is more effective and acceptable than standard psychiatric care, also the use of artificial nutrition and dietary management alone are both unacceptable as a primary interventions and ineffective as a form of relapse prevention, the overall conclusion is that therapies should have a full cooperation of the multidisciplinary medical and psychological teams specialized in eating disorders treatment.

## 6. Acknowledgment

The author would like to thank all the members of multidisciplinary team for their high professional work.

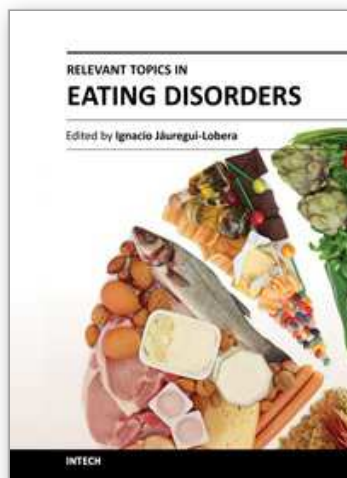
The author acknowledges the Fondazione FOBAN (obesity, bulimia, anorexia, nutrition) which supported the preparation of this manuscript.

## 7. References

- American Academy of Pediatrics. (2003). Committee on Adolescence. Identifying and treating eating disorders. *Pediatrics*, 111(1): 204-211.
- American Dietetic Association. (2011). Nutrition intervention in the treatment of eating disorders. *J Am Diet Assoc*, 111: 1236-1241.
- American Psychiatric Association. (2006). Work Group on Eating Disorders. Practice Guideline for the treatment of Patients with Eating Disorders. DOI. 10.1176/appi.books.9780890423363.138660.
- Bankhead, R., Boullata, J., Brantley, S., Corkins, M., Guenter, P., Krenitsky, J., Lyman, B., Metheny, N.A., Mueller, C., Robbins, S. & Wessel, J. (2009). Enteral nutrition administration. In: A.S.P.E.N. enteral nutrition practice recommendations. *JPEN J Parenter Enteral Nutr*, 33: 149-58.
- Beumont, P., Hay, P., Beumont, D., Birmingham, L., Derham, H., Jordan, A., Kohn, M., McDermott, B., Marks, P., Mitchell, J., Paxton, S., Surgenor, L., Thornton, C.,



- Wakefield, A. & Weigall, S. (2004). Royal Australian and New Zealand College of Psychiatrists Clinical Practice Guidelines Team for Anorexia Nervosa. Australian and New Zealand clinical practice guidelines for the treatment of anorexia nervosa. *Aust N Z J Psychiatry* Sep; 38(9):659-70.
- Birmingham, L. (2008). Managing Eating Disorders: The Refeeding Syndrome. *The Canadian Journal of Diagnosis*, 85-89.
- Gentile, M.G., Manna, G.M., Ciceri, R. & Rodeschini, E. (2008). Efficacy of inpatient treatment in severely malnourished anorexia nervosa patients. *Eat Weight Disord*, 13: 191-7.
- Gentile, M.G., Pastorelli, P., Ciceri, R., Manna, G.M. & Collimedaglia, S. (2010). Specialized refeeding treatment for anorexia nervosa patients suffering from extreme undernutrition. *Clin Nutr*, 29:627-632.
- Golden, N.H. & Meyer, W. (2004). Nutritional rehabilitation of anorexia nervosa. Goals and dangers. *Int J Adolesc Med Health*, 16: 131-44.
- Hearing, S.D. (2004). Refeeding Syndrome. *BMJ*, 328: 908-9.
- Lochs H., Allison, S.P., Meier, R., Pirlich, M., Kondrup, J., Schneider, St., van den Berghe, G. & Pichard, C. (2006). Introductory to the ESPEN Guidelines on Enteral Nutrition: Terminology, Definitions and General Topics. *Clinical Nutrition*, 25:180-186.
- Marinella, M.A. (2005). Refeeding Syndrome and Hypophosphatemia. *J Intensive Care Medicine*, 20: 155-59.
- Mehanna, H.M., Moledina, J. & Travis, J. (2008). Refeeding syndrome: what it is, and how to prevent and treat it. *BMJ*, 336: 1495-98.
- National Institute for Clinical Excellence, (2004). Eating Disorders. Core Interventions in the treatment and management of anorexia nervosa, bulimia nervosa and related eating disorders. [www.nice.org.uk](http://www.nice.org.uk)
- Paccagnella, A., Mauri, A., Baruffi, C. et al. (2006). Application criteria of enteral nutrition in patients with anorexia nervosa: Correlation between clinical and psychological data in a "lifesaving" treatment. *J Parenter Enter Nutr*, 30:231-239.
- Robb, A.S., Silber, T.J., Orrell-Valente, J.K. et al. (2002). Supplement nocturnal nasogastric refeeding for better short-term outcome in hospitalised adolescent girls with anorexia nervosa. *Am J Psychiatry*, 159: 1347-1353.
- Stanga, Z., Field, J., Iff, S., Stucki, A., Lobo, S.N. & Allison, S.P. (2007). The effect of nutritional management on the mood of malnourished patients. *Clin Nutr*, 26: 379-82.
- Stanga, Z., Brunner, A., Leuenberger, M., Grimble, R.F., Shenkin, A., Allison, S.P. & Lobo, D.N. (2008). Nutrition in clinical practice - the refeeding syndrome: illustrative cases and guidelines for prevention and treatment. *Eur J Clin Nutr*, 62: 687-94.
- Tonoike, T., Takahashi, T., Watanabe, H., Kimura, H., Suwa, M., Akaho. & Itaku, Y. (2004). Treatment with intravenous hyperalimentation for severely anorectic patients and its outcome. *Psych Clin Neurosci*, 58: 229-235.
- Zuercher, J.N., Cumella, E.J., Woods, B.K., Eberly, M. & Carr J.K. (2003). Efficacy of voluntary nasogastric tube feeding in female inpatients with anorexia nervosa. *JPEN J Parenter Enteral Nutr* Jul-Aug; 27(4):268-76.



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Edited by Prof. Ignacio Jáuregui Lobera

ISBN 978-953-51-0001-0

Hard cover, 390 pages

**Publisher** InTech

**Published online** 22, February, 2012

**Published in print edition** February, 2012

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